PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Amersham Biosciences AB
Patents Department
Björkgatan 30
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Sverige

DUE DATE:	Dec. 13. 2005	
FORMALITIES:	C.N ✓	PP ✓
PAT. OFF:	A.K	✓
ON DB	17/10	05
CASE NO:	PU0378-PCT	

PCT

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rule 66)

Date of mailing *(day/month/year)*	14-10-2005
Applicant's or agent's file reference: PU0378-PCT ✓	REPLY DUE: within 60 days from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE2004/001583 ✓	01.11.2004 ✓	31.10.2003

International Patent Classification (IPC) or both national classification and IPC
B01D 15/08, B01J 20/28, B01J 20/30

Applicant
Amersham Biosciences AB et al

1. ☒ The written opinion established by the International Searching Authority:
   ☒ is ☐ is not
   considered to be a written opinion of the International Preliminary Examining Authority.

2. This second (first, etc.) opinion contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

   When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(e).

   How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

   Also For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*. For an informal communication with the examiner, see Rule 66.6. For an additional opportunity to submit amendments, see Rule 66.4.

   If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary report on patentability (Chapter II of the PCT) must be established according to Rule 69.2 is: 28.02.2006

Name and mailing address of the IPEA/SE	Authorized officer
Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. 46 8 667 72 88	Lars Wallentin / MRo Telephone No. 46 8 782 25 00

Form PCT/IPEA/408 (cover sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/SE2004/001583

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:

- ☐ international search (Rules 12.3(a) and 23.1(b))
- ☐ publication of the international application (Rule 12.4(a))
- ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this opinion has been established on the basis of *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."):*

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ the claims:

pages _____ as originally filed/furnished
pages _____ as amended (together with any statement) under Article 19
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to the sequence listing *(specify)*: _____

WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/SE2004/001583

Box No. V **Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-3,5-7,9,10,16-19,32,34-36,38,
	Claims	39,45-51,53
Inventive step (IS)	Claims	1-3,5-7,9-14,16-19,32-43,45-53
	Claims	
Industrial applicability (IA)	Claims	
	Claims	

2. Citations and explanations:

The invention relates to a chromatography separation matrix, wherein the ligands provide a chemical gradient in the support. This leads to improved mass transport properties during adsorption and desorption.

The most relevant documents cited in the International Search Report are:

D1: US6426315B1
D2: US5561097A
D3: US6528322B1
D4: US5977345A

Document D1 relates to a process for preparing multifunctional porous separation matrices by introducing different functionalities in different layers of the matrix (see column 2, line 1-45; column 6, line 17-26). The process includes contacting a separation matrix that comprises reactive groups with a reagent (e.g. activating agent), the amount of which is not sufficient for reaction with all groups present in the matrix. Desired functionality can be introduced in a subsequent step. The substitution degree of one ligand in one layer is often different from the substitution degree for the same ligand in another layer. A ligand in the surface layer can be zero and at the same time present in another layer. Also the reverse can be true. Suitable matrices are in the form of particles (see column 3, line 47 - column 4, line 38). Charged ligands can be used (see column 4, line 57 - column 5, line 25).

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

The invention according to claims 1-3, 5-7, 9, 10, 16-19, 32, 34-36, 38, 39, 45-51 and 53 lacks novelty in view of D1.

The remaining claims 11-14, 33, 40-43 and 52 are considered to involve particular detail executions obvious to a person skilled in the art. Therefore, the invention according to these claims is not considered to involve an inventive step.

Claims 33 and 37 relates to two methods of coupling ligands to the separation matrix. These methods are not disclosed in D1. However, they are both known through D2. The fist method is disclosed in the background art of D3 (see column 1, line 22-26) and the second method is disclosed in the detailed description (see column 3, line 58-66 and column 5, line 24-35). The use of these methods in the invention according to claims 33 and 37 has not been shown to give rise to any unexpected effects. It is therefore considered to be obvious for a person skilled in the art to use the methods described in D2 in order to produce a matrix with a ligand density gradient as disclosed in D1. Consequently, the invention according to claims 33 and 37 lacks an inventive step.

The invention also lacks novelty in view of document D3. D3 discloses an analytical method for determination of two analytes in a sample by thin layer chromatography. The separation zone may have different ligand densities or a gradient of ligand densities along the separation direction.

The invention according to claims 1, 3, 10, 47, 49, 50 and 53 lacks novelty in view of D3.

See also D4 which discloses chromatographic affinity matrices with higher concentration of ligand or ionic moiety on the intra-particle volume than the outer matrix surface. See the abstract and claims.

The invention according to claims 1-3, 11-14, 16-19 and 47-53 lacks novelty in view of D4.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The term "solvent controlled diffusion" used in claim 20 is vague and unclear and leave the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).

Claim 40 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result should be added.

Claim 37 relates to independent claim 32 and the steps (a)-(c). These steps can not be replaced by a single step as defined in claim 37 as it would conflict with the independent claim 32.